

The Amendments to the Specification

Please amend the paragraph at page 3, lines 1-6 as follows:

One polymer that can be used for making stent coatings for local drug delivery can be selected from a group of poly(ester amides) described in U.S. Patent No. 6,503,538 to Chu et al. However, some ~~mechanical properties, such as hardness~~ properties of the poly(ester amides) taught by Chu et al. may be insufficiently good for drug-eluting stent applications. For example, the drug permeabilities only encompass a certain range for these hydrophobic polymers. Additionally, the biocompatibility of poly(ester amides) with hydrophilic, non-fouling moieties can be greater than those without. Accordingly, there is a need to have poly(ester amides) with better properties to allow the poly(ester amides) to be used ~~to make~~ in stent coatings for local drug delivery.

Please amend the paragraph at page 5, line 13 through page 6, line 25 as follows:

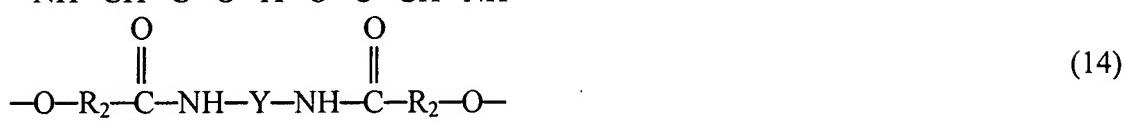
According to another aspect of the present invention, a medical article is provided, the article comprises an implantable substrate having a coating, the coating includes a copolymer having a general formula (10) or (11):



wherein, M can be a moiety represented by the structure having the formula (12):



P can be one of the moieties having the formulae (13), (14), (15), and (16):



Q can be one of the moieties having the formulae having the formulae (17), (18), and (19):

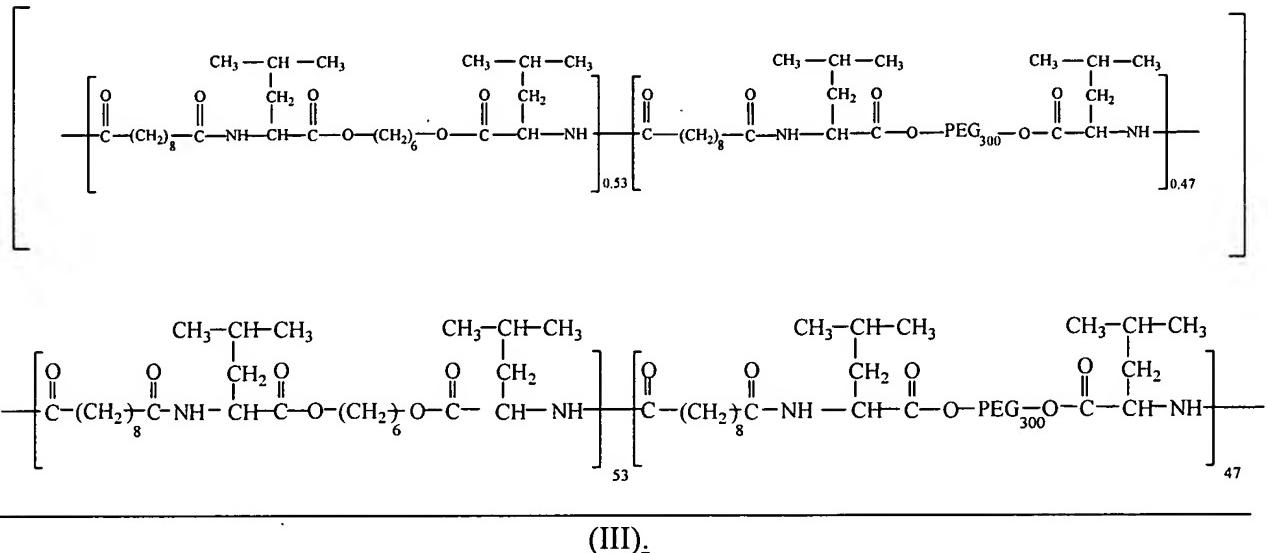


and M₁ can be a moiety represented by the formula (20):



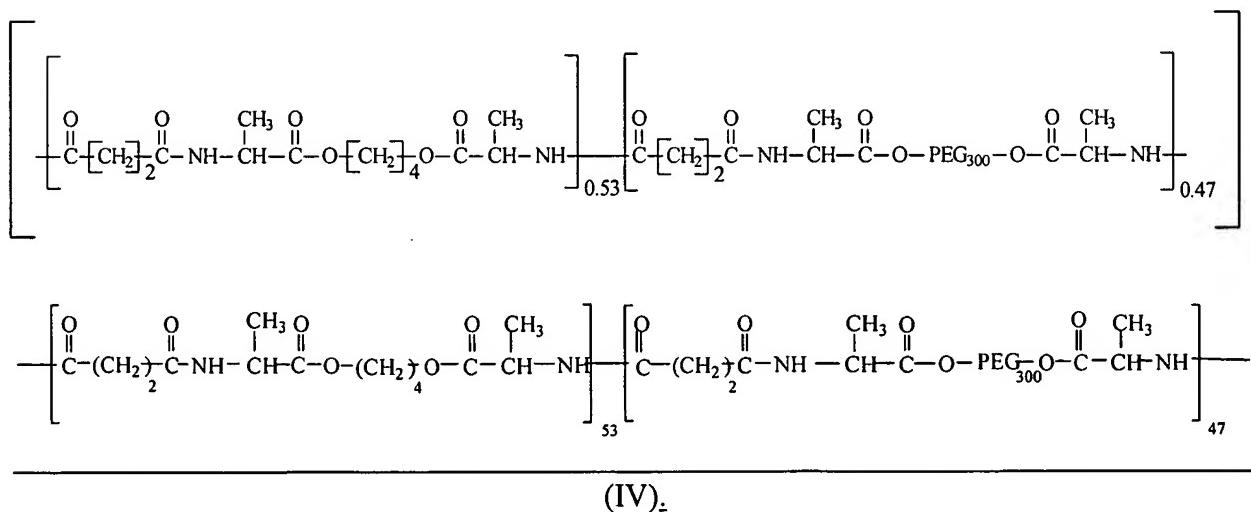
Please amend the paragraph at page 29, lines 1-4 as follows:

A copolymer having formula (III) can be synthesized and used in practice of the invention:



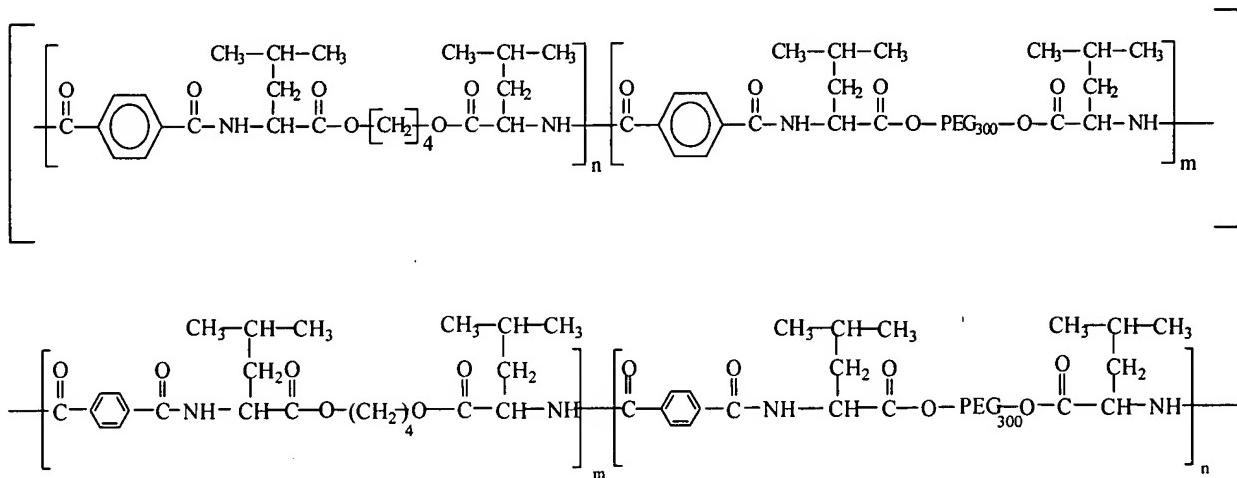
Please amend the paragraph at page 30, line 8 as follows:

A copolymer having formula (IV) can be synthesized and used in practice of the invention.



Please amend the paragraph at page 31, line 15 through page 32, line 2, as follows:

A copolymer having formula (V) can be synthesized and used in practice of the invention.



(V)_z

Please amend the paragraph at page 32, lines 10-14 as follows:

The copolymer (V) can be obtained using the same synthetic technique as described in Example 2 for copolymer (IV), except di-*para*-nitrophenylterephthalate can be used to make the copolymer (V), instead of di-*para*-nitrophenyl succinate. In copolymer (V), the value of *n* can be between about 0.64 64 and about 0.97 97 and the value of *m* can be between about 0.03 3 and about 0.36 36, where *m* + *n* = + 100.

Please amend the paragraph at page 33, lines 10-14 as follows:

The copolymer (VI) is a product of copolymerization of reagents A₁, B₂, and C₁. A₁ can be a diol-diamine shown in Table 1 where R₁ is *i*-C₄H₉ and X is (CH₂)₆. In other words, A₁ can be synthesized by condensation of leucine with 1,6-hexaanediol 1,6-hexanediol. B₂ can be a PEG-amidediol shown in Table 4 where R₂ is methylmethylen CH(CH₃)₂.

Please amend the paragraph at page 33, lines 14-16 as follows:

C₁ can be a dicarboxylic acid shown in Table 5 where R₃ is (CH₂)₈ (sebacic acid, which is also shown in Table 6). In copolymer (VI), the value of n can be between about 0.60 60 and about 0.93 93 and the value of m can be between about 0.07 7 and about 0.40 (m + n = 1) 40, where m + n = 100.

Please amend the paragraph at page 34, lines 2-5 as follows:

The copolymer (VII) can be synthesized in same way as the copolymer (VI) of Example 4, except instead of a reagent B₂ (e.g., PEG-amidediol), reagent B₄ (e.g., PEG-diamine) shown in Table 4 can be used. In copolymer (VII), the value of n can be between about 0.59 59 and about 0.96 96 and the value of m can be between about 0.04 4 and about 0.41 41, where m + n = 100.

Please amend the paragraph at page 35, lines 2-3 as follows:

C₁ can be a dicarboxylic acid shown in Table 5 where R₃ is (CH₂)₈ (sebacic acid, which is also shown in Table 6). In copolymer (VIII), the value of n can be between about 0.86 86 and about 0.99 99 and the value of m can be between about 0.01 1 and about 0.14 14, where m + n = 100.

Please amend the paragraph at page 35, lines 14-15 as follows:

The copolymer (IX) can be synthesized in same way as the copolymer (VIII) of Example 6, except instead of a reagent B₁ (PEG-diester-diamine), reagent B₂ (PEG-amidediol) shown in Table 4 can be used, where R₂ is methylmethylen CH(CH₃). In other words, B₂ can be synthesized by condensation of lactic acid with PEG-diamine shown as reagent B₄ in Table 4. PEG-diamine can be based on poly(ethylene glycol) having molecular weight of about 600 Daltons, which is symbolized by the abbreviation PEG₆₀₀. In copolymer (IX), the integer value of n can be between about 0.69 69 and about 0.98 98 and the value of m can be between about 0.02 2 and about 0.31 31, where m + n = 100.

Please amend the paragraph at page 36, lines 13-15 as follows:

Optionally, instead of a C₁ diacid, a dichloride of the diacid can be used, for instance, sebacyl dichloride. In copolymer (X), the value of n can be between about 0.54 54 and about 0.96 96 and the value of m can be between about 0.04 4 and about 0.46 46, where m + n = 100.

Please amend the paragraph at page 37, lines 5-10 as follows:

The copolymer (XI) can be synthesized in same way as the copolymer (X) of Example 9, except instead of a reagent B₃ (e.g., PEG-diol), reagent B₄ (such as PEG-diamine) shown in Table 4 can be used. PEG-diamine can be based on poly(ethylene glycol) having molecular weight of about 600 Daltons, which is symbolized by the abbreviation PEG₆₀₀. In copolymer (XI), the value of n can be between about 0.03 3 and about 0.35 35 and the value of m can be between about 0.97 97 and about 0.65 65, where m + n = 100.

Please amend the paragraph at page 38, lines 1-7 as follows:

The copolymer (XII) can be synthesized in same way as the copolymer (VIII) of Example 6, except instead of a reagent A₂ (amidediol), a reagent A₃ (diol) shown in Table 1 can be used, where X is (CH₂)₆. In other words, 1,6-hexanediol can be used as the reagent A₃. A poly(ethylene glycol) moiety having molecular weight of about 300 Daltons can comprise a part of copolymer (XII), which is symbolized by the abbreviation PEG₃₀₀. In copolymer (XII), the value of n can be between about 0.98 98 and about 0.71 71 and the value of m can be between about 0.02 2 and about 0.29 29, where m + n = 100.

Please amend the paragraph at page 38, lines 18-19 as follows:

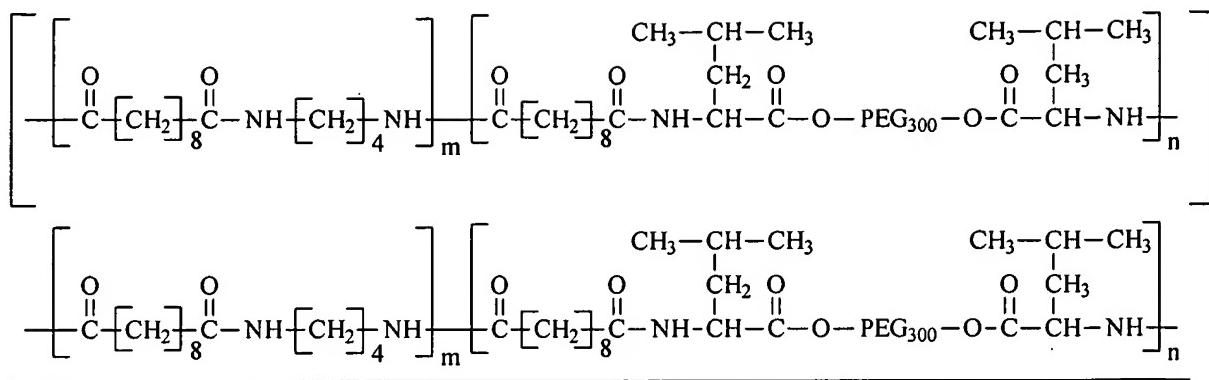
In copolymer (XIII), the value of n can be between about 0.98 98 and about 0.76 76 and the value of m can be between about 0.02 2 and about 0.24 24, where m + n = 100.

Please amend the paragraph at page 39, lines 14-15 as follows:

In copolymer (XIV), the value of n can be between about 0.98 98 and about 0.73 73 and the value of m can be between about 0.02 2 and about 0.27 27, where m + n = 100.

Please amend the paragraph at page 39, line 17 through page 40, line 1 as follows:

A copolymer having formula (XV) can be synthesized and used in practice of the invention.



(XV),

Please amend the paragraph at page 40, lines 9-10 as follows:

In copolymer (XV), the value of n can be between about 0.98 98 and about 0.73 73 and the value of m can be between about 0.02 2 and about 0.27 27, where m + n = 100.

Please amend the paragraph at page 41, lines 3-4 as follows:

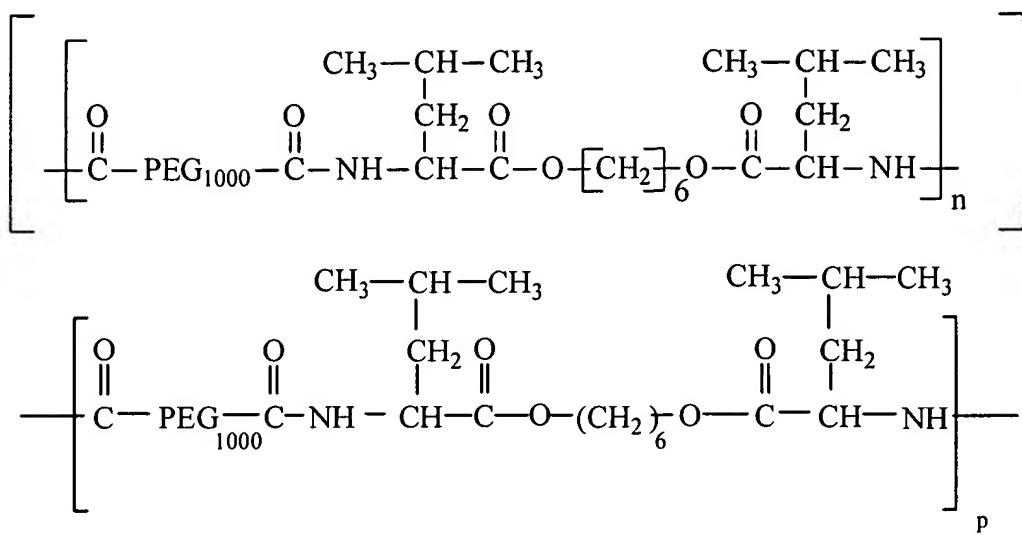
In copolymer (XVI), the value of n can be between about 0.98 98 and about 0.77 77 and the value of m can be between about 0.02 2 and about 0.23 23, where m + n = 100.

Please amend the paragraph at page 41, lines 15 and 16 as follows:

In copolymer (XVII), the value of n can be between about 0.995 995 about 0.91 910 the value of m can be between about 0.005 5 and about 0.09 90, where m + n = 1000.

Please amend the paragraph at page 42, lines 1-3 as follows:

A copolymer having formula (XVIII) can be synthesized and used in practice of the invention.



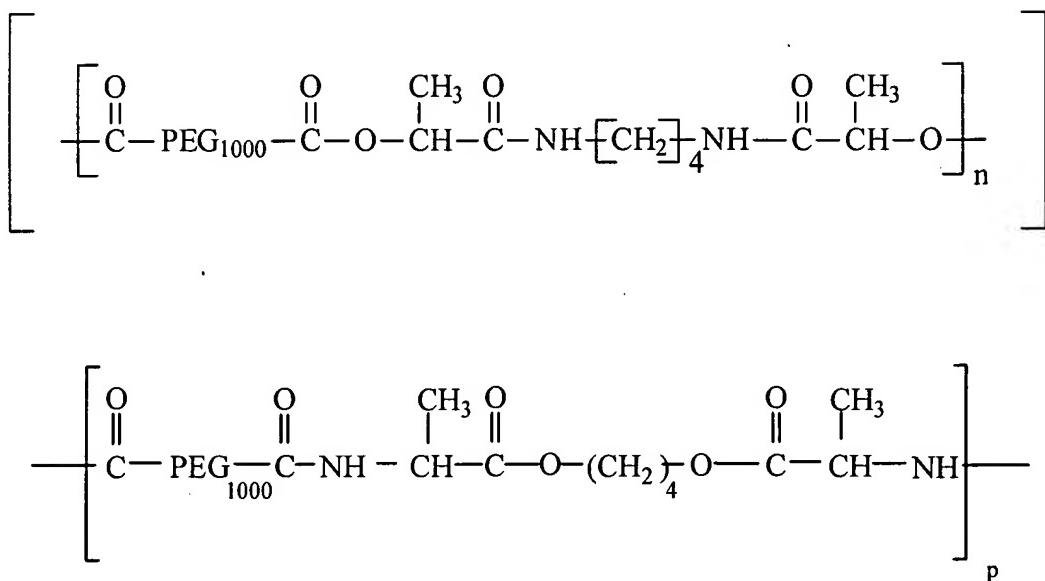
(XVIII).

Please amend the paragraph at page 42, lines 4-12 as follows:

To synthesize the copolymer (XVIII), reagents A₁ and C₂, can be combined in the molar ratio of about 1:1 and copolymerized. The conditions for the synthesis can be determined by those having ordinary skill in the art. A₁ can be a diol-diamine shown in Table 1 where R₁ is *i*-C₄H₉ and X is (CH₂)₆. In other words, A₁ can be synthesized by condensation of leucine with 1,6-hexanediol. C₂ can be a PEG-dicarboxylic acid shown in Table 5, derived from poly(ethylene glycol) having molecular weight of about 1,000 Daltons, which is symbolized by the abbreviation PEG₁₀₀₀. A total molecular weight of the copolymer (XVIII) can be between about 20,000 Daltons and about 50,000 Daltons. The value of the integer n p can be between about 14 and 360.

Please amend the paragraph at page 42, lines 14-17 as follows:

A copolymer having formula (XIX) can be synthesized and used in practice of the invention.



(XIX).

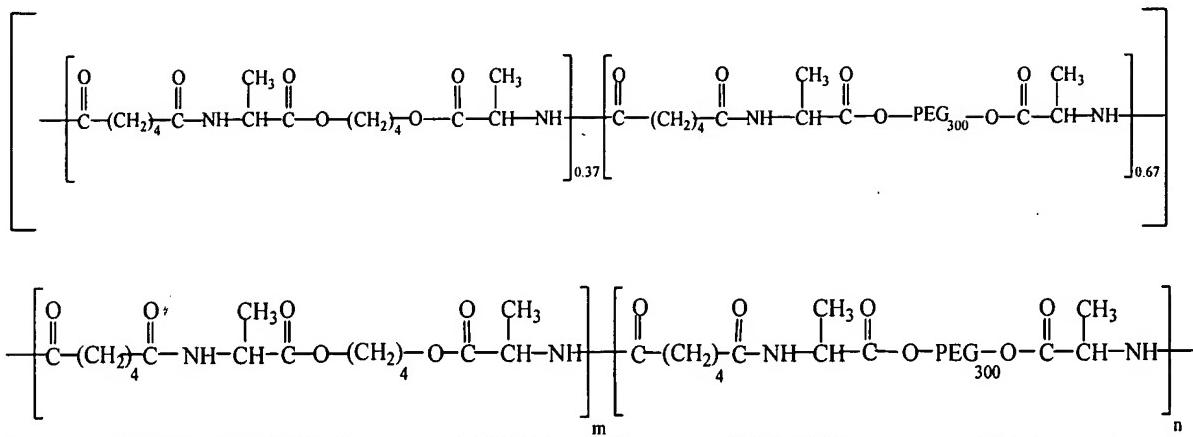
Please amend the paragraph at page 43, lines 6-7 as follows:

A total molecular weight of the copolymer (XIX) can be between about 20,000 Daltons and about 50,000 Daltons. The value of the integer n p can be between about 15 and 390.

Please amend the paragraph at page 43, lines 9-13 as follows:

~~Co-poly-[N,N'-adipoyl-bis-(L-alanine)-1,4-butylene diester]_{0.37}-[N,N'-adipoyl-bis-(L-alanine)-PEG300 diester]_{0.67}}~~ Co-poly-{[N,N'-adipoyl-bis-(L-alanine)-1,4-butylene diester]₃₇₋
[N,N'-adipoyl-bis-(L-alanine)-PEG300 diester]₆₇} having formula (XX) can be synthesized and

used in practice of the invention. This copolymer belongs to category (A), type A₁-B₁-C₁, described above.



(XX)_z

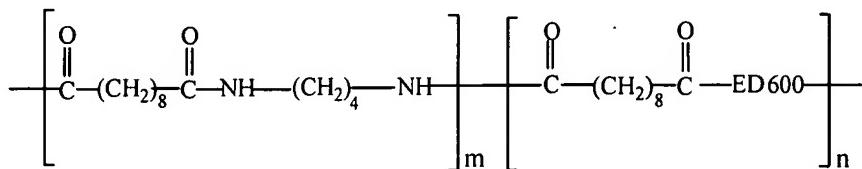
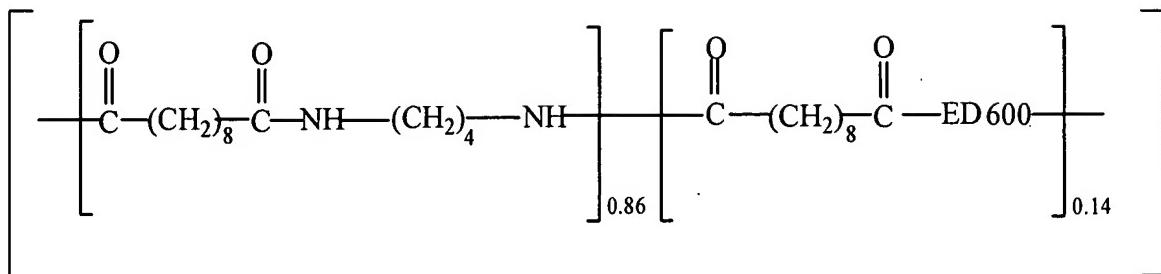
Please amend the paragraph at page 44, lines 14-17 as follows:

For example, the final polymer can contain between about 5 mass % and about 50 mass % of PEG. For copolymer (XX), this corresponds to molar ratios of the two blocks of (alanine/butanediol-adipic acid) (A₁-C₁ blocks) and (alanine/PEG-adipic acid) (B₁-C₁ blocks) between about 0.94:0.06 94:6 and about 0.12:0.88 12:88.

Please amend the paragraph at page 44, line 19 through page 45, line 2 as follows:

~~Co-poly-[N,N'-sebacyl-1,4-butylene diamide]₈₆-[N,N'-sebacyl-(ED-600) diamide]₁₄}~~

Co-poly-[{[N,N'-sebacyl-1,4-butylene diamide]₈₆-[N,N'-sebacyl-(ED-600) diamide]₁₄} having formula (XXI) can be synthesized and used in practice of the invention. This copolymer belongs to category (B), type (A₄-B₄-C₁), described above.



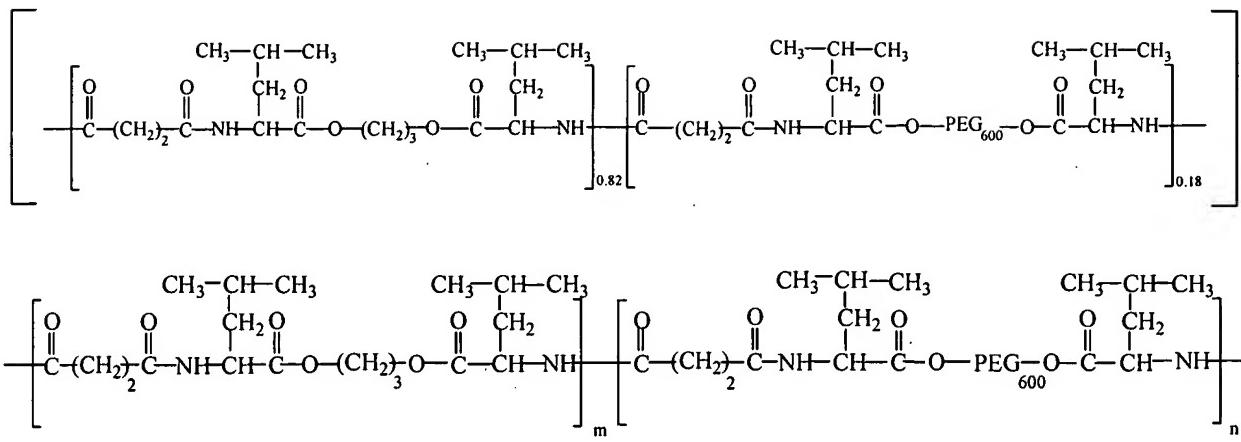
(XXI)

Please amend the paragraph at page 45, line 17 through page 46, line 4 as follows:

As only amide bonds are present, without any other hydrolysable groups, harsher synthetic conditions can be used for this category as understood by those having ordinary skill in the art. For example, acid chlorides can be used. The mass contents of PEG in the final copolymer (XXI) can be between about 5 mass % and about 50 mass %. For copolymer (XXI), this corresponds to molar ratios of the two blocks of (diamine-sebacic acid) (A_4-C_1 blocks) and (ED-600-sebacic acid) (B_4-C_1 blocks) between about 0.97:0.03 97:3 and about 0.57:0.43 57:43.

Please amend the paragraph at page 46, lines 6-10 as follows:

~~Co-poly-[N,N'-succinyl-bis-(L-leucine)-1,3-propylene diester]_{0.82}-[succinyl-PEG600 diester]_{0.18}~~ Co-poly-{[N,N'-succinyl-bis-(L-leucine)-1,3-propylene diester]₈₂-[succinyl-PEG600 diester]₁₈} having formula (XXII) can be synthesized and used in practice of the invention. This copolymer belongs to category (C), type ($A_1-B_3-C_1$), described above.



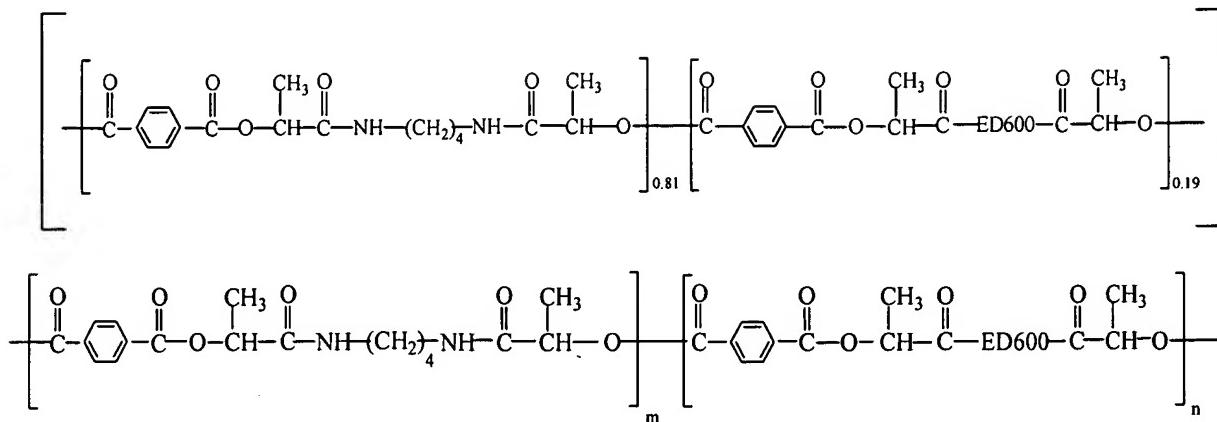
Please amend the paragraph at page 47, lines 10-16 as follows:

In this category, both amide and ester bonds are present in the copolymer. Accordingly, mild conditions need be used, as understood by those having ordinary skill in the art. For example, carboxylate groups activated by carbodiimides can be used or good leaving groups such as *para*-nitro-phenol can be used. The mass contents of PEG in the final copolymer (XXII) can be between about 5 mass % and about 50 mass %. For copolymer (XXII), this corresponds to molar ratios of the two blocks of (leucine/propanediol-succinic acid) (A₁-C₁ blocks) and (PEG-diol-succinic acid) (B₃-C₁ blocks) between about 0.94:0.06 94:6 and about 0.12:0.88 12:88.

Please amend the paragraph at page 47, line 18 through page 48, line 2 as follows:

~~Co-poly-[terephthalyl-bis-(D,L-lactate)-1,4-butylene diamide]_{0.84}-[terphthalyl-bis-(glycolate)-ED600-diamide]_{0.19}}~~ Co-poly-{[terephthalyl-bis-(D,L-lactate)-1,4-butylene diamide]₈₁-[terphthalyl-bis-(glycolate)-ED600 diamide]₁₉} having formula (XXIII) can be

synthesized and used in practice of the invention. This copolymer belongs to category (D), type (A₂-B₂-C₁), described above.



(XXIII).

Please amend the paragraph at page 48, line 13 through page 49, line 2 as follows:

In this category, only ester bonds present in the copolymer. Amide bonds may, or may not, be present in the reagents. Accordingly, transesterification reactions, under dehydrating conditions, in the presence of the Lewis or Bronsted acid catalysts can be used. Use of acid chlorides is also a viable synthetic technique because the only hydrolysable bonds that may be present in the reagents are stable amide bonds. The mass contents of PEG in the final copolymer (XXIII) can be between about 5 mass % and about 50 mass %. For copolymer (XXIII), this corresponds to molar ratios of the two blocks of (A₂-C₁ blocks) (B₂-C₁ blocks) between about 0.97:0.03 97:3 and about 0.49:0.51 49:51.

Please amend the paragraph at page 49, lines 4-11 as follows:

A first composition can be prepared, the composition including:

(a) between about 1.0 mass % and about 15 mass %, for example, about 2.0 mass % ~~eo-poly {[N,N'-sebacyl bis (L-leucine)-1,6-hexylene diester]}_{0.75}-[N,N'-sebacyl-L-lysine benzyl ester]}~~_{0.25} co-poly-{[N,N'-sebacyl-bis-(L-leucine)-1,6-hexylene diester]}₇₅-[N,N'-sebacyl-L-lysine benzyl ester]}₂₅;

(b) between about 0.1 mass % and about 2.0 mass %, for example, about 0.5 mass% paclitaxel; and

(c) the balance, a solvent blend of ethanol and 1,1,2-trichloroethane, where the mass ratio between ethanol and 1,1,2-trichloroethane can be about 1:1.

Please amend the paragraph at page 50, lines 12-16 as follows:

A first composition can be prepared by mixing the following components:

(a) between about 1.0 mass % and about 15 mass %, for example, about 2.0 mass% copolymer ~~eo-poly {[N,N'-sebacyl bis (L-leucine)-1,6-hexylene diester]}_{0.75}-[N,N'-sebacyl-L-lysine 4-amino-TEMPO amide]}~~_{0.25} co-poly-{[N,N'-sebacyl-bis-(L-leucine)-1,6-hexylene diester]}₇₅-[N,N'-sebacyl-L-lysine-4-amino-TEMPO amide]}₂₅; and

(b) the balance, 100% ethanol.

Please amend the paragraph at page 51, lines 11-16 as follows:

A third composition can be prepared by mixing the following components:

(a) between about 0.5 mass % and about 10 mass %, for example, about 1.0 mass% copolymer (XX) described in Example 18;

- (b) between about 0.5 mass % and about 10 mass %, for example, about 1.0 mass % ~~eo-poly {[N,N'-sebacyl bis (L-leucine)-1,6-hexylene diester]}_{0.75}-[N,N'-sebacyl-L-lysine benzyl ester]_{0.25}}~~ co-poly-{[N,N'-sebacyl-bis-(L-leucine)-1,6-hexylene diester]₇₅-[N,N'-sebacyl-L-lysine benzyl ester]₂₅} described in Example 22; and
- (c) the balance, 100% ethanol.